REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 1, 3-12, 15-19, 21, 39, 40, and 42-55 were pending. Claim 19 has been canceled without prejudice to future prosecution in a related application. Claims 56-101 have been added. Accordingly, claims 1, 3-12, 15-18, 21, 39, 40, and 42-101 are pending. Claims 1, 3, 18, 39, 42, 43, 47, and 50 have been amended to more clearly define certain embodiments of the present invention. Support for amendments to claims 1, 18, 39, 43, 47 and 50 may be found in paragraph [0006] of the published application for the added language related to distinguishing elements (*e.g.*, "said distinguishing element distinguishes said polynucleotide molecule from a genomic DNA or RNA molecule that is nearly identical to said polynucleotide molecule" in claim 1) and in Figures 2-5 for the language indicating that both the target nucleic acid sequence and the distinguishing element are in the same strand of a nucleic acid molecule of interest. All the remaining amendments to the previously pending claims are merely editorial. Support for new claims 56 and 78 may be found in paragraphs [0008] and [0046]. Support for new claim 57 may be found in paragraphs [0046] to [0050]. Support for new claims 58 and 79 may be found in paragraph [0051]. Support for new claims 59 and 80 may be found in paragraphs [0048] to [0052]. Support for new claims 60 and 81 may be found in paragraph [0051]. Support for new claims 61 and 82 may be found in paragraph [0103]. Support for new claims 63, 64, 83 and 84 may be found in paragraph [100]. Support for new claims 64 and 85 may be found in paragraph [0089]. Support for new claims 65-68 and 86-89 may be found in paragraphs [0089] and [0090]. Support for new claims 69 and 90 may be found in paragraph [0017]. Support for new claims 70 and 91 may be found in paragraphs [0060] and [0094]. Support for new claims 71, 72, 92 and 93 may be found in paragraph [0078]. Support for new claims 73, 74, 94 and 95 may be found in paragraph [0082]. Support for new claims 75, 76, 96 and 97 may be found in paragraph [0022]. Support for claim 77 may be found in paragraph [0008]. Support for new claims 98-101 may be found in paragraph [0023]. No new matter has been added by the above amendments.

Rejection Under 35 U.S.C. § 102

Claim 19 stands rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Engelhardt *et al.* (U.S. Patent No. 6,221,581).

Without agreeing with the above rejection or prejudice to future prosecution of this claim in a related application, Applicants have canceled this claim.

Claims 50-52 and 55 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Lundeberg *et al.* (U.S. Patent No. 6,482,592). More specifically, in the Action, it is asserted that Lundeberg *et al.* disclose a method for separating a polynucleotide molecule from a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (*i.e.*, module-binding site), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (module) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element (via additional modules, column 4, lines 9-11) and immobilizing the polynucleotide-targeting element-separation group complex and isolating the complex (column 11, lines 7-14).

Applicants respectfully traverse this ground of rejection to the extent applicable to the currently pending claims. Applicants submit that the '592 patent fails to disclose a method for separating a polynucleotide molecule (*i.e.*, a genomic DNA or RNA molecule) from a population of genomic DNA or RNA molecules wherein the polynucleotide molecule (*e.g.*, a gene of maternal origin) comprises *a distinguishing element that distinguishes itself from another genomic DNA or RNA molecule with a nearly identical sequence (*e.g., *the same gene of paternal origin).* More specifically, the '592 patent is directed to methods for improving the binding of a series of consecutive nucleotide bases to a complementary target nucleic acid molecule in a sample and their use in isolating primer extension products. It does not teach separating a genomic DNA or RNA molecule from a population that may contain another genomic DNA or RNA molecule with a nearly identical sequence. The '592 patent fails to disclose a target DNA that comprises a *distinguishing element* as recited in the currently pending claims located near the region to which an immobilized probe binds (*see*, Figure 3A of the '592 patent) or the

isolation of such a target DNA. Such a failure further results in the lack of description in this cited patent about selective stabilization of the binding of a targeting element-separation group to a target nucleic acid sequence that depends on the presence or absence of a distinguishing element near the target nucleic acid sequence to which the targeting element binds as claimed in the present application.

Claims 50-52 and 55 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Bukanov *et al.* (*PNAS 95*:5516-20, 1998). More specifically, in the Action, it is asserted that Bukanov *et al.* disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (*i.e.*, control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (*i.e.*, opposite strand), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (biotinylated oligonucleotide probe) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element via PNA opener and immobilizing the polynucleotide-targeting element-separation group (page 5517 to page 5518, left column).

Applicants respectfully traverse this ground of rejection to the extent applicable to the currently pending claims. The presently claimed methods are for separating a polynucleotide molecule one strand of which comprises both a target nucleic acid sequence and a distinguishing element. Such a feature is not disclosed in the Bukanov *et al.* reference because the homopurine tract is the alleged target nucleic acid sequence, and the alleged distinguishing element is the opposite strand of a homopurine tract. The failure in describing a distinguishing element near a target nucleic acid sequence in the same strand of a polynucleotide molecule in the Bukanov *et al.* reference results in the lack of description in this cited reference about about selective stabilization of the binding of a targeting element-separation group to a target nucleic acid sequence that depends on the presence or absence of a distinguishing element near the target nucleic acid sequence to which the targeting element binds as claimed in the present application.

In view of the above remarks, Applicants submit that this ground of rejections under 35 U.S.C. § 102(b) has been overcome. Withdrawal of these rejections is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1, 3-12, 15-18, 21, 39-40, and 42-49 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ju *et al.* (U.S. Patent No. 5,876,936) in view of Engelhardt *et al.* (U.S. Patent No. 6,221,581). More specifically, it is asserted in the Action that the '936 patent discloses a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (*i.e.*, mixture of differently sized primer extension products, column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of termination incorporation, column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (*i.e.*, primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated ddNTP) to the targeting element bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (column 7, lines 5-32; column 9, lines 36-53 and claim 18, steps a-g). It is also asserted that the '581 patent teaches a similar method of separating a polynucleotide (claims 112-116) wherein the DNA encompasses any DNA, and further teaches that the method is useful for detecting SNPs and that SNPs are important elements of genomic DNA (column 2, lines 17-23; column 3, lines 22-45; and column 12, lines 26-50). It is concluded in the Action that it would have been obvious to one of ordinary skill in the art at the time of the present invention to apply the SNP separation/detection of the '581 patent to the genomic DNA analysis of the '936 based on the known importance of SNPs to separate and detect important genomic DNA as suggested by the '581 patent.

Applicants respectfully traverse this ground of rejection to the extent applicable to the claims as amended. First, the '936 patent and the '581 patent, alone or in combination, fail to teach or suggest the methods currently claims in the present application. More specifically, the '936 patent and the '581 patent, alone or in combination, fail to teach or suggest selective

attachment of a separation group to a targeting element as recited in the presently pending claims. The '936 patent does not describe a method that requires that attachment of a separation group (*e.g.*, a biotinylated nucleotide) to a targeting element (*e.g.*, an oligonucleotide) occurs *only* if a distinguishing element as recited in the presently pending claims is present. Instead, this patent describes a method in which a primer/oligonucleotide is bound to a target nucleic acid at a primer binding site adjacent to a site of terminator incorporation, and the primer/oligonucleotide is extended in the presence of nucleotides that include a biotinylated nucleotide. In the Action, it is asserted that the primer/oligonucleotide corresponds to the targeting element recited in the claims, the primer binding site adjacent the site of terminator incorporation corresponds to the distinguishing element, and that the biotinylated nucleotide corresponds to the separation group. Because according to the '936 patent deoxynucleotides are present along with biotinylated dideoxynucleotides, incorporation of biotinylated dideoxynucleotides will occur as long as there is a matching nucleotide anywhere downstream of the primer binding site, it thus does not depend on the presence or the absence of a distinguishing element (*e.g.*, a SNP) as recited in the presently pending claims.

The lack of disclosures about selective attachment of a separation group to a targeting element *only* in the presence of the combination of a target nucleic acid sequence (*i.e.*, primer binding site in the '936 patent) and a distinguishing element in the '936 patent has not been remedied by the '581 patent. More specifically, there are no descriptions in the '581 patent about selective attachment of a separation group to a targeting element that depends on the presence or absence of a distinguishing element near the location to which the targeting element binds in a nucleic acid molecule of interest. Should this rejection be maintained, Applicants respectfully request that specific sections in the '581 patent where such descriptions are provided be identified.

Second, Applicants submit that no sufficient motivation is present for one of ordinary skill in the art to combine the '936 patent with the '581 patent to obtain the presently claimed subject matter. More specifically, the '936 patent is directed to improving the accuracy and clarity of sequencing analyses. As one skilled in the art would know, for sequencing reactions to produce accurate and clear results, the starting DNA sample needs to be of high

purity. It other words, the starting DNA sample should or preferably contain only a DNA molecule of interest that is able to anneal with a sequencing primer, not other DNA molecules with similar sequences that are also able to anneal to the sequencing primer. The presence of such other DNA molecules would produce signals that interfere with those produced from the DNA molecule of interest. Combining the '936 patent with the '581 patent as asserted in the Action would require that the '936 patent be modified for separating a DNA molecule of interest from other DNA molecules in a starting DNA sample, including another DNA molecule that is nearly identical to the DNA molecule of interest and to which a primer for sequencing the DNA molecule of interest also anneals. The use of such a starting DNA sample would defeat or at least frustrate the purpose of the '936 patent, that is, to improve clarity and accuracy of sequencing analysis.

Third, there is no reasonable expectation of success for one of ordinary skill in the art to combine the '936 patent and the '581 patent to produce the currently claimed invention. The '936 patent, as discussed in Applicants' previous response, describes a method using cloned template DNA. DNA amplified by PCR or cloned DNA would be expected to be present in several orders of magnitude greater copy numbers relative to an uncloned DNA or RNA, which is required by the claims. A sufficiently high copy number is clearly necessary for the identification of sequencing reaction products in order to obtain any detectable signal with standard sequencing systems. It should be obvious to someone skilled in the art that if such a sequencing reaction as described in the '936 patent were to be carried out on genomic DNA, the desired locus would first need to be amplified with a method such as PCR. There is no indication, however, that this method could be adapted for a target nucleic acid that has not been cloned, as is required by the claims. A declaration by Robert S. Ingram is submitted to this effect.

Claims 53 and 54 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bukanov *et al.* (*PNAS 95*:5516-20, 1998) in view of Engelhardt *et al.* (U.S. Patent No. 6,211,581). More specifically, it is asserted in the Action that (1) the Bukanov *et al.* reference discloses a method of separating a polynucleotide molecule from a population of nucleic acid

molecules with all the features recited in previously pending claim 50 on which claims 53 and 54 depend, (2) the '581 patent teaches a similar method of separating a polynucleotide, its use in detecting SNPs, and the importance of SNPs, and (3) it would have been obvious to one of ordinary skill in the art at the time of the present invention to apply the SNP separation/detection of the '581 patent to the genomic DNA analysis of the Bukanov *et al.* reference based on the known importance of SNPs to separate and detect important genomic DNA as suggested by the '581 patent.

Applicants respectfully traverse this ground of rejection. As discussed above, the Bukanov *et al.* reference fails to disclose selective stabilization of the binding of a targeting element-separation group to a target nucleic acid sequence that depends on the presence or absence of the distinguishing element near a target nucleic acid sequence to which the targeting element binds. Also as discussed above, such a deficiency has not been remedied by the '581 patent. Accordingly, the Bukanov *et al.* reference and the '581 patent, alone or in combination, fail to teach or suggest the subject matter as recited in claims 53 and 54 of the present application.

Claims 53 and 54 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Lundeberg *et al.* (U.S. Patent No. 6,482,592) in view of Engelhardt *et al.* (U.S. Patent No. 6,211,581). More specifically, it is asserted in the Action that (1) the '592 patent discloses a method of separating a polynucleotide molecule from a population of nucleic acid molecules with all the features recited in previously pending claim 50 on which claims 53 and 54 depend, (2) the '581 patent teaches a similar method of separating a polynucleotide, its use in detecting SNPs, and the importance of SNPs, and (3) it would have been obvious to one of ordinary skill in the art at the time of the present invention to apply the SNP separation/detection of the '592 patent to the genomic DNA analysis of the '592 patent based on the known importance of SNPs to separate and detect important genomic DNA as suggested by the '581 patent.

Applicants respectfully traverse this ground of rejection. As discussed above, the '592 patent fails to disclose selective stabilization of the binding of a targeting element-

separation group to a target nucleic acid sequence that depends on the presence or absence of the distinguishing element near a target nucleic acid sequence to which the targeting element binds. Also as discussed above, such a deficiency has not been remedied by the '581 patent. Accordingly, the Bukanov *et al.* reference and the '581 patent, alone or in combination, fail to teach or suggest the subject matter as recited in claims 53 and 54 of the present application.

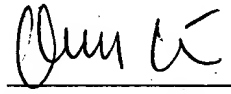
In view of the above remarks, Applicants submit that this ground of rejections under 35 U.S.C. § 103(a) has been overcome. Withdrawal of these rejections is respectively requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application (*i.e.*, claims 1, 3-12, 15-18, 21, 39, 40, and 42-101) are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Enclosure:
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